AMENDMENTS TO THE CLAIMS

The following is a complete listing of the claims in the application including the present status thereof and including any amendments made by this paper. In this paper, new claims 115-125 have been added.

Listing of claims:

1-55(canceled).

56(previously presented). A method of treatment of a chronic inflammatory disease in a patient, the method comprising the administration to the patient of a compound that selectively inhibits T_{ck} cells.

57(previously presented). A method according to claim 56 wherein said compound is a nucleic acid molecule encoding a polypeptide which selectively inhibits T_{ck} cells.

58(previously presented). A method according to claim 56 wherein said compound selectively inhibits T_{ck} cell-induced release of one or more pro-inflammatory cytokines from monocytes.

59(previously presented). A method according to claim 58 wherein the cytokine is tumour necrosis factor-∀.

60(previously presented). A method according to any one of claims 56-59 wherein said compound selectively inhibits NF-6B.

61(previously presented). A method according to any one of claim 56-59 wherein said compound selectively activates PI3 kinase.

62(previously presented). A method according to claim 60 wherein the nucleic acid molecule encodes an NF-kB inhibitor, preferably I6B∀.

63(previously presented). A method according to claim 61 wherein the nucleic acid molecule encodes an NF-kB inhibitor, preferably I6B∀.

64(previously presented). A method of identifying a compound with efficacy in the treatment of a chronic inflammatory disease comprising the step of testing the compound for an ability to selectively inhibit T_{ck} cells.

65(previously presented). A method according to claim 64 wherein testing the compound for an ability to selectively inhibit T_{ck} cells comprises testing the compound for an ability to selectively inhibit T_{ck} cell-induced release of one or more pro-inflammatory cytokines from monocytes.

66(previously presented). A method according to claim 65 wherein the cytokine is tumour necrosis factor-∀.

67(previously presented). A method according to claim 66 wherein said method comprises the following steps:

(i) pre-incubating monocytes with a compound to be tested;

(ii) resuspending said pre-incubated monocytes in the absence of the test compound;

(iii) stimulating said resuspended monocytes by co-culturing with either T_{ck} cells or T_{tcr} cells; and

(iv) assaying for TNF∀ production by said stimulated monocytes.

68 (previously presented). A method according to claim 66 wherein said method comprises the following steps:

(i) pre-incubating separate cultures of T_{ck} cells and T_{tcr} cells with a compound to be tested either prior to fixation or during their activation in culture;

(ii) resuspending said T_{ck} cells and T_{tcr} cells in the absence of the test compound;

(iii) stimulating monocytes by co-culturing with said resuspended T_{ck} cells or T_{tcr} cells; and

(iv) assaying for TNF∀ production by said stimulated monocytes.

69 (previously presented). A method according to any one of claims 64-68 wherein the chronic inflammatory disease is a disease of humans.

70 (previously presented). A method according to claim 69 wherein the chronic inflammatory disease is rheumatoid arthritis.

71(previously presented). A method according to claim 64 wherein testing the compound for an ability to selectively inhibit T_{ck} cells or selectively inhibit T_{ck} cell-induced release of one or more pro-inflammatory cytokines from monocytes comprises determining whether the compound exhibits NF-6B inhibition.

72(previously presented). A method according to claim 71 wherein NF-6B inhibition is constituted by a reduction in the binding of nuclear extracts, derived from monocytes exposed to the compound, to an NF-6B promoter DNA oligonucleotide.

73(previously presented). A method according to claim 72 wherein a reduction in the binding of nuclear extracts, derived from monocytes exposed to the compound, to an NF-6B promoter DNA oligonucleotide is determined by an electrophoretic mobility shift assay (EMSA).

74(previously presented). A method according to any one of claims 71-73 wherein NF-6B inhibition is deemed to exist if the binding of NF-6B to an NF-6B promoter DNA oligonucleotide is reduced to no more than 50%, a presumption being strengthened as that percentage approaches zero.

75(previously presented). A method according to claim 71 wherein NF-6B inhibition is constituted by a reduction in expression of the NF-6B gene.

76(previously presented). A method according to claim 75 wherein a reduction in the expression of the NF-6B gene is determined by a reporter gene assay.

77(previously presented). A method according to claim 76 wherein the reporter gene assay comprises coupling a ∃-galactosidase gene to the NF-6B gene and determining a reduction in ∃-galactosidase activity.

78(previously presented). A method according to claim 77 wherein ∃-galactosidase activity is reduced to no more that 50%.

79(previously presented). A method according to claim 64 wherein testing the compound for an ability to selectively target T_{ck} cells or selectively inhibit T_{ck} cell-induced release of one or more pro-inflammatory cytokines from monocytes comprises determining whether the compound exhibits PI3 kinase activation.

80(previously presented). A method according to claim 79 wherein PI3 kinase activation is constituted by an increase in PI3 kinase activity in monocytes exposed by the compound.

81(previously presented). A method according to claim 80 wherein PI3 kinase activation is deemed to exist if there is an increase in PI3 kinase activity equivalent to a range from at least 50% of the increase induced by IL-10 stimulation

(100 ng/ml for 2 minutes), to an amount greater than the increase induced by IL-10 stimulation.

82(previously presented). A compound identified as having efficacy in the treatment of a chronic inflammatory disease by testing the compound for an ability to selectively inhibit T_{ck} cells or selectively inhibit T_{ck} cell-induced release of one or more pro-inflammatory cytokines from monocytes.

83(previously presented). An antibody-like molecule having specificity for T_{ck} cells.

84(previously presented). An antibody-like molecule according to claim 83 selected from the group of molecules consisting of Fab molecules, $F(ab^1)_2$ molecules, Fv molecules, disulphide-linked Fv molecules, single chain Fv (scFv) molecules and single domain antibodies (dAbs).

85(previously presented). An antibody-like molecule according to claim 83 wherein said antibody-like molecule is humanized.

86(previously presented). An antibody-like molecule according to claim 84 wherein said antibody-like molecule is humanized.

87(previously presented). A method of making an antibody-like molecule having specificity for T_{ck} cells.

88(previously presented). An isolated cell that expresses an antibody-like molecule having a specificity for T_{ck} cells.

89(previously presented). An isolated cell according to claim 88 wherein the cell is a hybridoma cell.

90(previously presented). A method for identifying an antibody-like molecule having specificity for T_{ck} cells comprising the following steps:

(i) providing a population of T_{ck} cells; and

(ii) using said T_{ck} cells to screen a library of antibody-like molecules.

91(previously presented). A method according to claim 90 wherein the antibody-like molecule library is a phage display library.

92(previously presented). A compound comprising a target cell specific portion and a directly or indirectly cytotoxic portion, wherein the target cell specific portion comprises an antibody-like molecule having a specificity for T_{ck} cells.

93(previously presented). A compound according to claim 92 wherein the antibody-like molecule is selected from the group of molecules consisting of Fab molecules, $F(ab^1)_2$ molecules, Fv molecules, disulphide-linked Fv molecules, single chain Fv (scFv) molecules and single domain antibodies (dAbs).

94(previously presented). A compound according to claim 93 wherein said antibody-like molecule is humanized.

95(previously presented). A compound according to any one of claims 92-94 wherein the cytotoxic portion is a directly cytotoxic portion selected from the group consisting of radionuclides, ricin, ribonuclease, deoxyribonuclease, and *Pseudomonas* exotoxin A.

96(previously presented). A compound according to any one of claims 92-94 wherein the cytotoxic portion is indirectly cytotoxic.

97(previously presented). A compound according to any one of claims 92-94 wherein the cytotoxic portion is capable of inducing apoptosis of the target cells.

98(previously presented). A compound according to any one of claims 92-94 wherein the cytotoxic portion is an enzyme.

99(previously presented). A compound according to claim 97 wherein the cytotoxic portion is an enzyme.

100(previously presented). A compound according to any one of claims 92-94 wherein the target cell specific portion and the cytotoxic portion are fused.

101(previously presented). A compound according to claim 100 wherein the target cell specific portion and the cytotoxic portion are separated by a linker sequence.

102(previously presented). A compound according to any one of claims 92-94 having a nucleic acid molecule encoding.

103(previously presented). A compound according claim 101 having a nucleic acid molecule encoding.

104(previously presented). A compound according to any one of claims 92-94 wherein said nucleic acid molecule is included in a vector.

105(previously presented). A compound according to claim 103 wherein said nucleic acid molecule is included in a vector.

106(previously presented). A compound according to claim 104 wherein said vector is included in a host cell line.

107(previously presented). A compound according to claim 105 wherein said vector is included in a host cell line.

108(previously presented). A compound according to claim 82 for use in the treatment of a chronic inflammatory disease.

109(previously presented). A preparation of T-cell enriched cells wherein the cells are from tissue from a site of inflammation in a patient suffering from a chronic inflammatory disease.

110(previously presented). A preparation of cells according to claim 109 wherein the chronic inflammatory disease is rheumatoid arthritis.

111(previously presented). A preparation of cells according to claim 109 wherein the tissue is from the synovium.

112(previously presented). A preparation of cells according to claim 110 wherein the tissue is from the synovium.

113(previously presented). A preparation of cells according to any one of claims 109-112 wherein the T-cell enriched cells are CD3+-enriched cells.

114(previously presented). A preparation of cells according to any one of claims 109-112 wherein the T-cell enriched cells are non-adherent cells.

115(new). A method of identifying a compound with efficacy in the treatment of chronic inflammatory disease comprising the step of testing the compound for an ability to selectively inhibit the ability of Tck cells to induce pro-inflammatory cytokine release from a monocyte.

116(new). A method according to claim 115 wherein said compound is an antibody or an antibody-like molecule having specificity for Tck cells.

117(new). A method according to claim 115 wherein said method comprises the following steps:

(i) pre-incubating Tck cells with a compound to be tested;

(ii) optionally resuspending said Tck cells in the absence of the test compound;

(iii) co-culturing said Tck cells with monocytes; and

(iv) assaying for the production of pro-inflammatory cytokines by said monocytes.

118(new). A method according to claim 115 wherein said pro-inflammatory cytokine is TNFα.

119(new). A method according to claim 90 further comprising the steps of:

(iii) selecting one or more antibody-like molecule(s) from said library which selectively bind said Tck cells;

(iv) pre-incubating a population of Tck cells with said antibody-like molecule(s);

(v) co-culturing said population of Tck cells with monocytes; and

(vi) assaying for TNFα produced by said monocytes.

120(new). A method according to claim 115 wherein said Tck cells are produced by incubating a population of T cells with one or more cytokines.

121(new). A method according to claim 115 wherein said Tck cells are isolated from synovial tissue.

122(new). A method according to claim 115 wherein said Tck cells are capable of stimulating release of one or more pre-inflammatory cytokines from monocytes.

123(new). A method of identifying a compound with efficacy in the treatment of chronic inflammatory disease comprising the steps of:

(i) incubating a population of T cells with one or more cytokines to produce Tck cells; and

(ii) testing the compound for an ability to selectively inhibit the ability of the Tck cells to induce pro-inflammatory cytokine release from a monocyte.

124(new). A method according to claim 115 comprising determining whether the compound exhibits NF-κB activation.

125(new). A method according to claim 115 comprising determining whether the compound exhibits PI3 kinase activation.